



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : A61M 1/16, B01D 71/26, 71/54, 71/70, 61/00	A1	(11) International Publication Number: WO 00/38758 (43) International Publication Date: 6 July 2000 (06.07.00)
---	----	--

(21) International Application Number: PCT/IB99/02041
(22) International Filing Date: 22 December 1999 (22.12.99)

(30) Priority Data:
MI98A002831 24 December 1998 (24.12.98) IT

(71) Applicant (for all designated States except US): IN.TE.C.
S.R.L. [IT/IT]; Via Baccelli, 44, I-41100 Modena (IT).

(72) Inventor; and

(75) Inventor/Applicant (for US only): SCAGLIARINI, Raffaella
[IT/IT]; Corso Italia, 226, I-44043 Mirabello (IT).

(74) Agent: MODIANO, Guido; Modiano Gardi Patents, Via
Meravigli, 16, I-20123 Milan (IT).

(81) Designated States: JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published

With international search report.

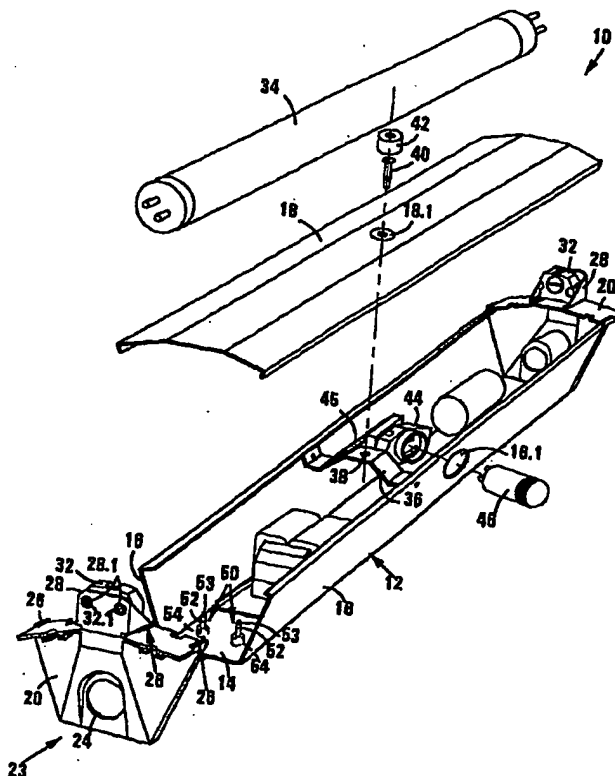
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

In English translation (filed in Italian).

(54) Title: USE OF A SELECTIVE MEMBRANE IN A BIOMEDICAL DEVICE FOR THE EXTRACORPOREAL TREATMENT OF BLOOD AND OTHER ORGANIC FLUIDS

(57) Abstract

The present invention relates to the use of a selective membrane (3) in a biomedical device (1) for the extracorporeal ozonization of blood and biological fluids. The device (1) used in the treatment comprises a hollow body (2) in which there are two compartments (blood compartment 4") for the passage of two fluids; the compartments are separated by a membrane (3) which is made of polymeric resin for the selective molecular diffusion of ozone and/or oxygen and is substantially inert with respect to ozone.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

USE OF A SELECTIVE MEMBRANE IN A BIOMEDICAL DEVICE FOR THE EXTRACORPOREAL TREATMENT OF BLOOD AND OTHER ORGANIC FLUIDS

TECHNICAL FIELD

5 The present invention relates to the use of a selective membrane in a biomedical device for the treatment of blood and biological fluids.

 In particular, the present invention relates to a biomedical device for the extracorporeal ozonization of blood or biological fluids and to the use of particular membranes in blood treatments performed outside the body.

10 BACKGROUND ART

 Ozone, the active principle used in the present invention, is an unstable gas currently applied as a whitening, oxidizing, and water purifying agent thanks to its disinfectant activity.

 In the medical field, during the last few decades ozone has found
15 different applications, from the disinfection of deep wounds of the limbs to the treatment of immune deficiencies and chronic obstructive vasculopathies.

 In particular, the validity of the administration of ozone in the treatment of various disorders is currently acknowledged by using it in a mixture with
20 oxygen and by applying it with different administration methods, which include:

 -- the intravenous pathway, which provides for the injection of ozone/oxygen mixtures of up to 180 cc per day. This method of administration is currently being abandoned because of the severe
25 pulmonary complications observed in a high percentage of treated cases;

 -- the intra-arterial pathway (femoral artery), which provides for the injection of up to 5 cc of O_2/O_3 (30-40 $\mu g/cc$). This method of administration associated with autohemotherapy is currently the treatment of election for chronic obstructive vasculopathies and allows to avoid 40%
30 of amputations in stage IV of arteriopathies of the lower limbs;

-- the subcutaneous and intramuscular pathway, which provides for the injection of up to 150 cc of O_2/O_3 (20-40 $\mu g/cc$). This method of administration has the drawbacks of being painful during the first minutes, of possibly causing embolization of the patient and of having mediocre patient compliance;

-- the intracavitary (intra-articular, peritoneal and pleural) pathway, which yields positive but anecdotal results;

-- the rectal pathway, by using a Teflon sound. Administration provides for the rectocolonic insufflation of 450-750 cc of gas (20-30 μg) for treating AIDS-related diarrhea, modest rectocolitis and chronic hepatitis. The main drawback of this form of administration is the empirical nature of the dosage, which does not allow to adjust the treatment dose with respect to the actual requirements of the patient;

-- the cutaneous or mucosal pathway, which provides for the treatment of the affected area, delimited hermetically beforehand with a containment bag, with a constant flow of O_2/O_3 (up to 80 $\mu g/cc$) for approximately 20 minutes, preventing the patient from inhaling O_3 . This procedure, especially if associated with autohemotherapy, is highly effective in the curing of chronic ulcerations of the lower limbs such as bedsores, venous and arterial vasculopathies, gangrenous injuries;

-- IV reinfusion of the blood of the donor, treated ex vivo with O_2/O_3 . This technique, known as autohemotherapy, consists in the ex vivo exposure of human blood to a mixture of ozone and oxygen for a short period of time, thus inducing an oxidative stress. The treated blood is then reinfused to the patient. The autohemotransfusion procedure has proved itself adequately safe, relatively low in cost and capable of justifying its use in various disorders.

This procedure, however, is not devoid of drawbacks in use, mainly due to the duration of the treatment, which entails withdrawal of a modest amount of blood (approximately 200-300 ml), insufflation of the mixture

based on oxygen and ozone and/or hydrogen peroxide, and subsequent reinfusion of the treated pouch.

Moreover, another drawback observed in autohemoperfusion is constituted by the impossibility to treat large volumes of blood or derivatives thereof in order to avoid drawing too much blood from the patient.

DISCLOSURE OF THE INVENTION

One of the aims of the present invention consists in avoiding or substantially attenuating the drawbacks observed in the prior art related to the extracorporeal ozonization of blood or biological fluids.

A principal object of the invention is to provide new uses for selective membranes in the field of extracorporeal treatments for the ozonization of blood, plasma or other biological fluids.

Another object of the present invention is to provide a biomedical device for the ozonization of blood or biological liquids allowing to perform an extracorporeal treatment on the entire blood volume in a short time and with a wide safety margin for the patient.

Another object of the present invention is to provide a biomedical device for the ozonization of human blood limiting the risks of embolism that occur in the direct insufflation of the mixture of gases into the circulatory system or into body tissues.

Another object of the invention is to provide a biomedical device for the extracorporeal ozonization of human blood or body liquids which can be manufactured with low production costs.

In view of these and other aims which will become apparent hereinafter there is provided, according to a first aspect of the present invention, the use of a membrane of polymeric resin which is permeable to ozone by molecular diffusion and is substantially inert with respect to ozone in the extracorporeal ozonization of blood or of a biological liquid.

The membranes used in the scope of the present invention are

membranes made of a polymeric resin which is resistant to the oxidative processes caused by contact with ozone and is selectively permeable to ozone or to a gas mixture containing ozone. The passage of the ozone gas occurs through the membranes by molecular diffusion according to the gas concentration gradient.

Particularly adapted polymeric resins are selected from the group that comprises resins of polyethylene, polyurethane, silicone, and combinations of layers of polyethylene/polyurethane/polyethylene resins.

From a structural point of view, the membranes used are hollow-fiber membranes or flat membranes.

Adapted hollow-fiber membranes are constituted by microporous capillaries having a thickness preferably between 40 and 60 μ and an average pore diameter preferably between 0.05 and 0.3 μ .

The microporosity of the membranes prevents the gas from passing in the form of microbubbles (microembolisms), which would damage plasma proteins.

Adapted flat membranes are non-microporous membranes preferably made of silicone with a thickness which is advantageously between 5 and 100 μ . Gas exchange through this type of membrane occurs by molecular diffusion and is proportional to the thickness of the membrane and to the gradient of concentration of the ventilated gas mixture.

Particularly adapted hollow-fiber membranes have a polyethylene content between 40 and 50%, more preferably equal to 45%, and a residual content of soy/castor oil of preferably less than 100 ppm.

In accordance with another aspect of the present invention, a biomedical device for the extracorporeal ozonization of blood and biological liquids is provided which comprises a hollow body in which there are two compartments for the passage of two fluids, these compartments being separated by a selective membrane, the device being characterized in that the selective membrane comprises at least one portion made of a polymeric

resin which is permeable to ozone by molecular diffusion and is substantially inert with respect to ozone.

The Applicant has now found that it is possible to obviate the drawbacks of the prior art observed in the reinfusion of blood with mixtures of oxygen and ozone by supplying one of the compartments of the device of the above-described type with blood or other biological fluid and the other compartment with ozone or a gas mixture containing ozone, so as to provide the transfer of the ozone from the compartment at high concentration to the compartment at lower concentration by molecular diffusion through the selective membrane.

The device according to the invention is provided with membranes of the hollow-fiber or flat-fiber type as described above.

In the device according to the invention, the ozone is preferably administered in a gaseous mixture with one or more physiologically tolerable gases, oxygen being the preferred one among these gases. The mixture of ozone is supplied at a pressure which is preferably between 0.1 and 0.3 bar.

The therapeutic concentration of O_3 in the gaseous mixture is advantageously between 5 and 40 $\mu\text{g/ml}$. It has been observed that the use of ozone at these levels of concentration facilitates the formation of ROS (reactive oxygen species), natural substances which activate different biological functions.

Moreover, ozone, as a strong oxidizing agent, can regulate the production of antioxidant intracellular enzymes, inhibiting the constant cellular oxidative stress that usually causes degenerative and aging-related disorders.

Another aspect of the present invention relates to the use of a device of the type described above in a method for the extracorporeal ozonization of blood, plasma or biological fluids.

During the use of the device according to the invention, an

extracorporeal stream of blood is pumped into one of the two compartments, while a gas mixture containing ozone is insufflated into the other compartment. The two streams of fluid advantageously flow in countercurrent.

5 For example, a stream of blood with a flow-rate of 100 ml/min and a stream of O_2/O_3 (O_3 concentration = 30 $\mu\text{g/ml}$) are circulated in countercurrent in an ozonization device in which the microporous membrane is constituted by a bundle of hollow polyethylene fibers.

This operating method allows to process, in approximately one hour, a
10 volume of blood which is equivalent to the entire blood volume of a patient, while obviating the risks of embolism that occur with methods that provide for the direct insufflation of the mixture of gas into the circulatory system.

Ozonization of the blood of the patient occurs by molecular diffusion of the oxygen/ozone mixture through the selective membrane.

15 BRIEF DESCRIPTION OF THE DRAWINGS

Further characteristics and advantages will become apparent from the description of a preferred but not exclusive embodiment of a biomedical device for the extracorporeal ozonization of blood and biological fluids, illustrated only by way of non-limitative example with the aid of the
20 accompanying drawing, which is a transverse sectional view of the device according to the invention.

WAYS OF CARRYING OUT THE INVENTION

With reference to the above-cited figure, a biomedical device 1 for the ozonization of blood or plasma is illustrated which comprises a substantially
25 cylindrical hollow body 2 inside which there is, in a substantially longitudinal position, a microporous membrane 3 of the hollow (capillary) fiber polyethylene type, which has an elongated shape and is fixed proximate to the ends 6 and 7 of the body 2 by poured polyurethane resin 15. The microporous membrane 3 is constituted by a bundle of polymeric
30 (polyethylene) microporous capillary fibers which allow the molecular

diffusion of the ozone towards the blood that flows in the adjacent flow compartment 4. The blood flow compartment 4 is delimited by the internal walls of the hollow body 2 and by the external surface of the capillary fibers 3.

5 The blood flow compartment 4 is supplied by a sterile cannula 12 which is connected, by means of a supply nozzle 8, to the inlet located at one end of the body of the device. A second cannula 13 for reinfusing the treated blood to the patient is connected by means of a second nozzle 9 which is arranged at the opposite end of the body 2 of the device 1.

10 The body of the device 1 is further provided with an inlet 10 and with an outlet 11 which are arranged proximate to the two ends for the connection of the microporous hollow fibers 3 to the system for feeding the oxygen/ozone mixture. This system is constituted by a feeder cannula 14 and by a discharge cannula 15 connected by means of nozzles to the body of
15 the device 1.

According to one embodiment, the compartment 4 is provided with one or more collection chambers (not shown), which are preferably provided with paths for connection to the outside.

20 The blood for supplying the device is drawn intravenously from a patient requiring treatment and is transferred to an extracorporeal treatment system. This system comprises a first sterile cannula for transferring the blood from the withdrawal needle to a feeder pump. A second cannula leads from the pump and connects to the nozzle 10 for feeding the blood flow compartment 4 of the ozonization device 1. At the same time, a mixture of oxygen/ozone
25 is insufflated into the microporous capillaries of the filtering membrane 3, so as to produce a stream of gas which flows inside the ozonization device in countercurrent with respect to the blood stream. The gas mixture for ozonization is administered by connecting, by means of a cannula 14, the delivery valve of a gas bottle (not shown) to the nozzle 10 arranged
30 proximate to the inlet of the filtering membrane. A second cannula 15,

connected to the discharge nozzle 11, conveys the gas that leaves the device to a gas recovery system (not shown). The illustrated extracorporeal treatment facilitates the formation of reactive oxygen species in the treated blood which act as natural activators for a large number of biological
5 functions.

The disclosures in Italian Patent Application No. MI98A002831 from which this application claims priority are incorporated herein by reference.

CLAIMS

1. Use of a membrane made of polymeric resin which is permeable to ozone by molecular diffusion and is substantially inert with respect to ozone in an extracorporeal treatment for the ozonization of blood or of a biological
5 fluid.

2. The use according to claim 1, wherein said polymeric resin is chosen from the group that consists of resins of polyethylene, polyurethane, silicone or adjacent layers of polyethylene/polyurethane/polyethylene resins.

10 3. The use according to claim 1 or 2, wherein said membranes are hollow-fiber or flat-fiber membranes.

4. The use according to claim 3, wherein said hollow-fiber membranes are microporous capillaries whose thickness is between 40 and 60 μ and whose average pore diameter is preferably between 0.05 and 0.3 μ .

15 5. The use according to claim 1 or 2, wherein said membranes are flat silicone membranes.

6. The use according to claim 5, wherein said flat membranes have a thickness between 5 and 100 μ .

7. A biomedical device for extracorporeal ozonization of blood and
20 biological fluids, comprising a hollow body in which there are two compartments for the passage of two fluids, said compartments being separated by a selective membrane, characterized in that said selective membrane comprises at least one portion made of a polymeric resin which is permeable to ozone by molecular diffusion and is substantially inert with
25 respect to ozone.

8. The device according to claim 7, characterized in that said selective membrane is constituted by a plurality of microporous hollow fibers.

9. The device according to claim 8, characterized in that said hollow fibers have a pore diameter of 0.05 to 0.3 μ .

30 10. The device according to claim 8 or 9, characterized in that said

hollow fibers have a thickness of 40 to 60 μ .

11. The device according to any one of claims 2 to 4, characterized in that said hollow fibers are joined in a bundle by means of a polyurethane resin adhesive.

5 12. The device according to any one of claims 8 to 11, characterized in that said hollow fibers are arranged along the central portion of said hollow body and are fixed, at its ends, by pouring polyurethane resin.

13. The device according to claim 7, characterized in that said polymeric resin is chosen from the group that comprises polyethylene, polyurethane
10 and mixtures thereof.

14. The device according to claim 7, characterized in that said polymeric resin contains 45% polyethylene.

15. The device according to claim 7, characterized in that said polymeric resin is constituted by adjacent layers of polyethylene/
15 polyurethane/polyethylene resin.

16. The device according to claim 7, characterized in that said selective membrane is a flat membrane.

17. The device according to claim 16, characterized in that said flat membrane has a thickness between 5 and 100 μ .

20 18. The device according to claim 16 or 17, characterized in that said flat membrane is made of silicone.

19. The device according to any one of claims 16 to 18, characterized in that said flat membrane is shaped like a pouch which is rolled up in a spiral.

20. Use of a device according to claims 7 to 19 for the extracorporeal
25 ozonization of blood, plasma or biological fluids.

21. The use according to claim 20, wherein ozone or a mixture of ozone with other physiologically compatible gases is administered.

22. The use according to claim 21, wherein a gaseous mixture containing ozone at a concentration of 5 to 40 μ g/ml is administered.

30 23. The use according to any one of claims 20-23, wherein the ozone is

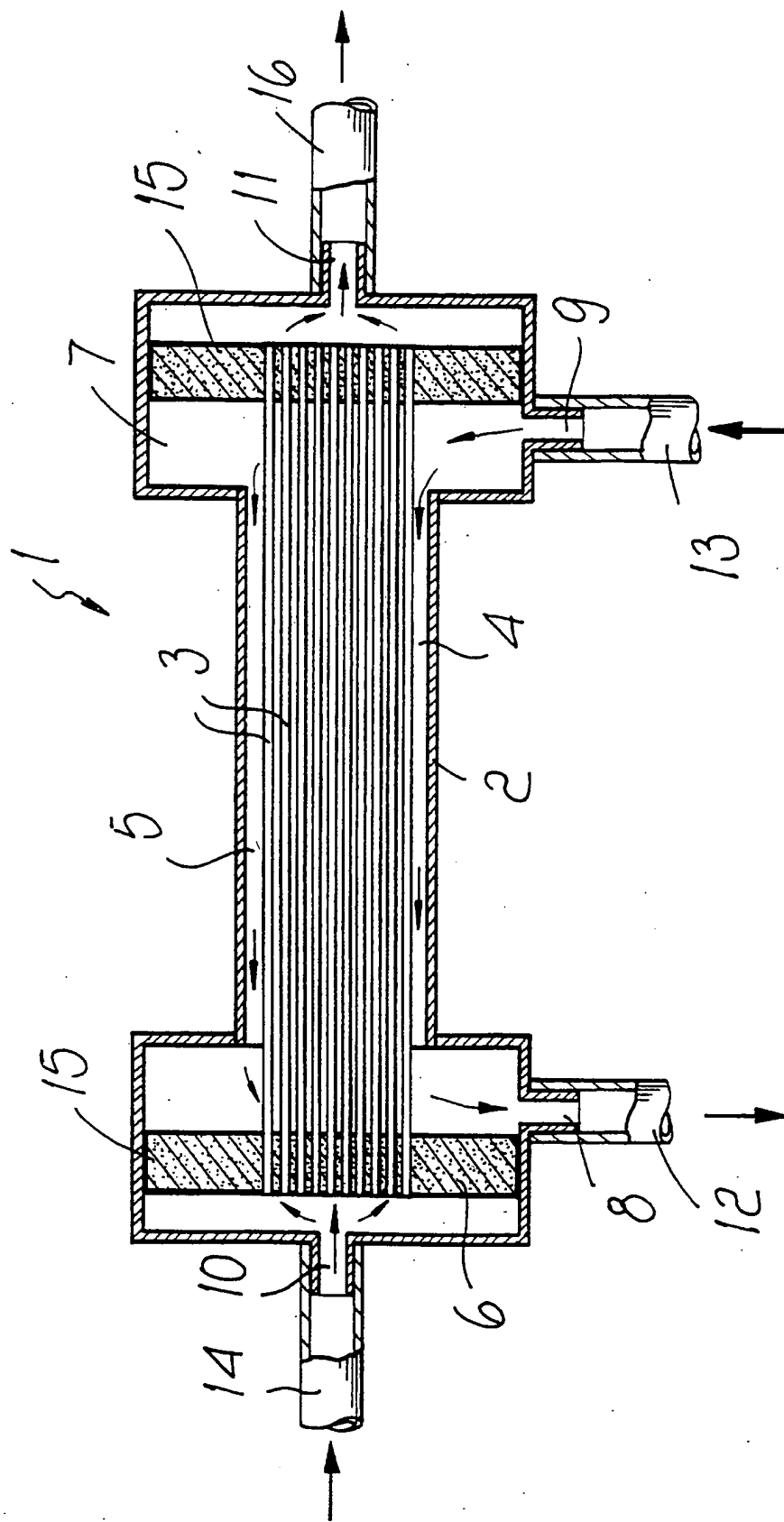
administered at a pressure between 0.1 and 0.3 bar.

24. The use according to any one of claims 20-23, wherein blood or a biological fluid flows in one compartment and a gaseous mixture comprising ozone flows in the other compartment.

5 25. The use according to claim 24, characterized in that said gaseous mixture is an O_3/O_2 mixture.

26. The use according to claim 24, wherein the blood or biological liquid and the gaseous mixture containing ozone flow in countercurrent.

1/1



INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 99/02041

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61M1/16 B01D71/26 B01D71/54 B01D71/70 B01D61/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61M B01D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 44 06 106 A (WERTH ULRICH DR MED) 31 August 1995 (1995-08-31) the whole document in particular, claims 1,3,6,7	1,3,7, 16,20, 21,24
Y	---	2,5,6
X	AU 637 374 B (MEDIZONE INTERNATIONAL INC) 27 May 1993 (1993-05-27) page 2, line 22 - line 32 page 3, line 7 -page 4, line 3	1,3,7,8, 20-26
Y	---	2,4
	-/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

17 May 2000

Date of mailing of the international search report

05/06/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Hoornaert, P

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 99/02041

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 025 256 A (MITSUBISHI RAYON CO) 23 January 1980 (1980-01-23) abstract; claims 1,4,5,7,9; figure 1 page 1, line 61 -page 3, line 21 page 3, line 56 - line 57 page 3, line 79 - line 83 page 4, line 22 - line 30 page 5, line 91 - line 126; example 5	7-10,13, 14
Y	---	2,4
X	TATSUMI E ET AL: "DEVELOPMENT OF AN INTEGRATED ARTIFICIAL HEART-LUNG DEVICE FOR LONG-TERM CARDIOPULMONARY SUPPORT" ASAIO JOURNAL,US,J.B.LIPPINCOTT CO.,HAGERSTOWN,MD, vol. 42, no. 5, 1 September 1996 (1996-09-01), pages M827-M832, XP000683650 ISSN: 1058-2916 page M828, column 1, last paragraph -column 2, line 18 figures 1,3	7-9, 11-13,15
Y A	---	2 14
X	KOLLA S ET AL: "TOTAL RESPIRATORY SUPPORT WITH TIDAL FLOW EXTRACORPOREAL CIRCULATION IN ADULT SHEEP" ASAIO JOURNAL,US,J.B.LIPPINCOTT CO.,HAGERSTOWN,MD, vol. 43, no. 5, 1 September 1997 (1997-09-01), pages 811-816, XP000728811 ISSN: 1058-2916 abstract page M812, column 1, last paragraph -column 2, line 3	7,16-19
Y	---	2,5,6
X	EP 0 167 162 A (TERUMO CORP) 8 January 1986 (1986-01-08) abstract page 1, paragraph 1 - paragraph 2 page 7, line 4 - line 27	7-13

	-/--	

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 99/02041

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>PATENT ABSTRACTS OF JAPAN vol. 1999, no. 01, 29 January 1999 (1999-01-29) -& JP 10 277370 A (NITTO DENKO CORP), 20 October 1998 (1998-10-20) abstract; figures paragraphs '0002!', '0027!', '0029!', '0031! -& DATABASE WPI Section Ch, Derwent Publications Ltd., London, GB; Class D15, AN 1999-012762 XP002137899 abstract</p>	7,16-19

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 99/02041

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 4406106 A	31-08-1995	NONE	
AU 637374 B	27-05-1993	AU 5627890 A	05-12-1991
GB 2025256 A	23-01-1980	JP 55001816 A	09-01-1980
		FR 2428456 A	11-01-1980
		NL 7904388 A	18-12-1979
		CA 1120870 A	30-03-1982
		US 4268279 A	19-05-1981
EP 0167162 A	08-01-1986	JP 1726540 C	19-01-1993
		JP 4000669 B	08-01-1992
		JP 61020559 A	29-01-1986
		AU 4451885 A	09-01-1986
		BE 902819 A	04-11-1985
		CH 364877 A	
		DE 3574341 D	28-12-1989
		FR 1208939 A	26-02-1960
		GB 902819 A	
		NL 233514 A	
		US 3029119 A	10-04-1962
JP 10277370 A	20-10-1998	NONE	